

IN THE SPECIFICATION

Please replace the paragraph beginning at page 9, line 11 of the specification as filed with the following (as per 37 C.F.R. §1.121(b)(1)(ii), the replacement paragraph is marked with underlines, strikethroughs, and brackets where appropriate):

--The surface active agent is optional and can be any pharmaceutically acceptable, non-toxic surfactant, e.g., polysorbate 80 (TWEEN® Tween 80), or the like. The surface-active agent may be present at a level of up to about 5 wt% and, preferably, from about 0.20 to about 2.0 wt%, based on the total weight of the granulation.--

Please replace the paragraph beginning at page 10, line 3 of the specification as filed with the following:

--The binders can be any pharmaceutically acceptable combination of non-toxic water soluble and water insoluble binders such as the following water-soluble polymers, e.g., polyvinyl alcohol, polyvinylpyrrolidone, methylcellulose, hydroxypropyl cellulose, hydroxymethyl cellulose, and the following water-insoluble polymers, e.g., a polymethacrylic acid copolymer such as ~~Eudragit~~ EUDRAGIT® NE30D. ~~Eudragit~~ EUDRAGIT® NE30D is commercially available as a 30% aqueous dispersion. Preferably, the subject formulation comprises the unique combination of both a water-soluble and water-insoluble binder up to about 10 wt % in an aqueous medium such as water, or as an aqueous dispersion. More preferably, the binder combination is provided from about 0.25 to 7.5 wt % based on the total weight of the granulation.--

Please replace the paragraph beginning on page 10, line 20 of the specification as filed with the following:

-- The enteric coating agent, if applied, can be any pharmaceutically acceptable material which resists acid up to a pH of about 5.0 or higher. Preferably, the enteric coating ingredient is selected from cellulose acetate phthalate, hydroxypropylmethyl cellulose phthalate, polyvinyl acetate phthalate, carboxymethylethylcellulose, ~~Eudragit~~ EUDRAGIT® NE30D, ~~Eudragit~~ EUDRAGIT® L (polymethacrylic acid:methylmethacrylate, 1:1 ratio; MW (No. Av. 135,000--USP Type A)) or ~~Eudragit~~ EUDRAGIT® S (polymethacrylic acid:methylmethacrylate, 1:2 ratio MW (No. Av. 135,000--USP Type B)) and, most preferably, can be a mixture thereof. For

example, Eudragit EUDRAGIT® L100-55 is a 100% polymer solids product while the Eudragit EUDRAGIT® L30-55 product is a 30% w/w aqueous dispersion of the polymer.--

Please replace the paragraph beginning on page 12, line 4 of the specification as filed with the following:

-- After the granulation is formed and dried, the granulation can be tableted by standard procedures as accepted in the art. The tablets can then be directly coated with the enteric coating agent, employing standard coating procedures. A color-imparting agent may be added to the enteric coating agent mixture or a rapidly dissolving seal coat containing color may be coated over the enteric coating agent layer provided that the seal coat is compatible with and does not affect the dissolution of the enteric coating layer. The rapidly dissolving seal coat can, for example, comprise Opadry OPADRY® pink which comprises approximately 91 wt % hydroxypropyl methylcellulose (E-6), color, and about 9 wt % polyethylene glycol applied as a 8-15% w/w solution in purified water. In addition, the color may be provided as "Chromateric" which is available from Crompton & Knowles. This product contains water, talc, TiO₂, triethyl citrate, propylene glycol, synthetic red iron oxide, potassium sorbate, xanthan gum, sodium citrate, and synthetic yellow iron oxide. If desired, conventional sugar based seal coats can be used which contain FDA-certified dyes...--

Please replace the paragraph beginning on page 12, line 19 of the specification as filed with the following:

-- A granulation comprising an acid-labile active ingredient (the "active ingredient granule") is formed in a fluid bed coater using a top spray granulation-forming suspension having micronized active ingredient, e.g., omeprazole. 5% w/w polyvinyl pyrrolidone; 2% w/w L-arginine; 0.5% w/w polysorbate 80; 0.4% w/w polymethacrylic acid copolymer, e.g., Eudragit EUDRAGIT® NE30D; and purified water. The suspension is sprayed onto a mixture of microcrystalline cellulose and 92% w/w of the total amount of L-arginine. The formulation for making the granulation using omeprazole as the active ingredient has the following composition.--

Please replace the table located at page 13 of the specification as originally filed with the following:

	Wt.	%
Povidone, USP (<u>PLASDONE® Plasidone K30</u>)	97.6g	5.37
Microcrystalline cellulose (<u>AVICEL® Avicel PH101</u>)	465.7g	25.62
L-arginine, USP/FCC	731.7g	40.25
Omeprazole, (USP, micronized) ¹	487.8g	26.84
Polysorbate 80	9.7g	0.53
Methylmethacrylic acid (<u>EUDRAGIT® Eudragit NE30D</u>)	25.2g	1.39

¹ 95% of the particles exhibit a particle size of less than 15 microns

Please replace the paragraph beginning at page 13, line 8 of the specification as filed with the following:

--The granulation is formed into tablets comprising 20 mg of active ingredient hereinafter, ("the omeprazole tablet") by standard tableting procedures. Specifically, the granules comprising omeprazole were mixed with Crospovidone and microcrystalline cellulose (Avicel AVICEL® PH101), then with glyceryl monostearate, in the following amounts:--

Please replace the paragraph on page 13, line 15 of the specification as filed with the following:

--Avicel AVICEL® PH 101 16.2g--

Please replace the paragraph beginning at page 14, line 12 of the specification as filed with the following:

--A granulation comprising an acid labile active ingredient is formed in fluid bed coater using a top spray granulation-forming suspension containing micronized active ingredient, e.g., omeprazole; 5%w/w of the total amount of L-arginine; polyvinyl pyrrolidone; sodium lauryl sulfate; a polymethacrylic acid copolymer, e.g., Eudragit EUDRAGIT® NE30D; and purified water. This suspension is sprayed onto a mixture of microcrystalline cellulose, 95%w/w of the total amount of L-arginine and sodium starch glycolate. The formulation for making the granulation has the following composition:--

Please replace the table beginning at page 14, line 19 of the specification as filed with the following:

	Wt.	%
Eudragit EUDRAGIT® NE30D	33.0g	1.81
Povidone, USP (PLASDONE® Plasidone K30)	98.0g	5.38
Sodium lauryl sulfate, NF/USP	6.0g	0.33
Microcrystalline cellulose (AVICEL® Avicel PH102)	463.0g	25.44
L-arginine, USP/FCC	732.0g	40.22
Omeprazole, (USP, micronized) ¹	488.0g	26.82
Purified water, USP	1600.0g	

¹ 95% of the particles exhibit a particle size of less than 15 microns

Please replace the paragraph beginning at page 15, line 5 of the specification as filed with the following:

--The granulation is formed into tablets containing 20mg of omeprazole by first mixing the omeprazole granules with crospovidone and microcrystalline cellulose (Avicel AVICEL® PH101), then with glyceryl monostearate, as follows:--

Please replace the paragraph at page 15, line 11 of the specification as filed with the following:

--Avicel AVICEL® PH101 16.2g--

Please replace the paragraph at page 16, line 6 of the specification as filed with the following:

--Opadry OPADRY® II pink 4.5g--

Please replace the paragraph beginning at page 16, line 11 of the specification as filed with the following:

--A granulation comprising an acid labile active ingredient was formed in fluid bed coater using a top spray granulation-forming suspension containing micronized omeprazole; 2.0% w/w of the total amount of L-arginine; polyvinyl pyrrolidone; polysorbate 80; and a polymethyl

methacrylic acid copolymer, e.g., Eudragit EUDRAGIT® NE30D. The suspension is sprayed onto a mixture of microcrystalline cellulose and 95.0% w/w of the total amount of L-arginine. The formulation for making the granulation has the following composition:--

Please replace the table on page 16 of the specification as filed with the following:

	Wt.	%
Povidone, USP (<u>PLASDONE® Plasdone K30</u>)	4.0g	4.77
Polysorbate 80 (<u>Tween TWEEN® 80</u>)	0.4g	0.48
<u>Eudragit EUDRAGIT® NE30D</u>	0.4g	0.48
L-arginine, USP/FCC	40.0g	47.73
Omeprazole, (USP, micronized) ²	20.0g	23.87
Microcrystalline cellulose (<u>AVICEL® Avicel PH102</u>)	19.0g	22.67

² 95% of the particles exhibit a particle size of less than 15 microns

Please replace the paragraph beginning at page 17, line 1 of the specification as filed with the following:

--The granulation is formed into tablets containing 20mg of omeprazole by first mixing the omeprazole granules with Crospovidone XL and Avicel AVICEL® PH102, then with glyceryl monostearate, as follows:--

Please replace the paragraph located at page 17, line 7 of the specification as filed with the following:

--Microcrystalline cellulose (Avicel AVICEL® PH102) 79.6mg--

Please replace the paragraph located at page 17, line 15 of the specification as filed with the following:

--Eudragit EUDRAGIT® L30D-55 14.0mg--

Please replace the paragraph located at page 17, line 16 of the specification as filed with the following:

--Color (ChromaterieCHROMATERIC®) 7.0mg--

Please replace the paragraph beginning at page 17, line 21 of the specification as filed with the following:

--A granulation comprising an acid labile active ingredient is formed in fluid bed coater using a top spray granulation-forming suspension containing micronized active ingredient, e.g., omeprazole; 2.0% w/w of the total amount of L-arginine; polyvinyl pyrrolidone; polymethylmethacrylic acid copolymer, e.g., Eudragit EUDRAGIT[®] NE30D; and purified water. The suspension is sprayed onto a mixture of microcrystalline cellulose and 95.0% w/w of the total amount of L-arginine. The formulation for making the granulation has the following composition, in mg/tablet:--

Please replace the table located on page 18 of the specification as filed with the following:

	Wt.	%
Povidone, USP (<u>PLASDONE</u> [®] <u>Plasdone</u> K30)	2.0g	5.42
Eudragit <u>EUDRAGIT</u> [®] NE30D	0.16g	0.43
Polysorbate 80	0.2g	0.54
L-arginine, USP/FCC	15.01g	40.65
Omeprazole, (USP, micronized) ³	10.0g	27.09
Microcrystalline cellulose (<u>AVICEL</u> [®] <u>Avicel</u> PH101)	9.55g	25.87

³ 95% of the particles exhibit a particle size of less than 15 microns

Please replace the paragraph beginning at page 18, line 8 of the specification as filed with the following:

--The granulation is tableted into tablets containing 10mg of active ingredient, e.g., omeprazole, by first mixing the omeprazole granules with sodium starch glycolate and Avicel AVICEL[®] PH102, then with glycetyl monostearate:--

Please replace the paragraph located at page 18, line 14 of the specification as filed with the following:

--Microcrystalline cellulose (Avicel AVICEL[®] PH102) 118.9mg--

Please replace the table located on page 19 of the specification as filed with the following:

	Wt.	%
Povidone, USP (<u>PLASDONE® Plasidone K30</u>)	8.00mg	5.42
Polymethacrylic acid copolymer	0.62mg	0.42
Polysorbate 80	0.80mg	0.54
L-arginine, USP/FCC	60.0mg	40.65
Omeprazole, (USP, micronized) ⁴	40.0mg	27.10
Microcrystalline cellulose	38.18mg	25.87
Purified water, USP	n/a	

4 95% of the particles exhibit a particle size of less than 15 microns

Please replace the table located on page 20 of the specification as filed with the following:

Omeprazole tablets (prepared above)	124.00mg
<u>Eudragit EUDRAGIT® L30D-55</u>	17.00mg
1M NaOH (pH adjuster to pH 5.0)qs	Na
Acetyl tributyl citrate	1.70mg
Talc	3.80mg
Polysorbate 80	1.50mg
Purified water qs	na

Please replace the paragraph beginning at page 21, line 5 of the specification as filed with the following:

--A granulation comprising an antidiabetic active ingredient is formed in fluid bed coater using a top spray granulation-forming suspension containing active ingredient, e.g., glipizide; polyvinyl pyrrolidone; sodium lauryl sulfate; a polymethacrylic acid copolymer, e.g., Eudragit EUDRAGIT® NE30D; and purified water. This suspension is sprayed onto a mixture of

microcrystalline cellulose, 95%w/w of the total amount of sodium starch glycolate. The formulation for making the granulation has the following composition:--

Please replace the table located on page 21 of the specification as filed with the following:

	Wt.	%
Eudragit <u>EUDRAGIT® NE30D</u>	33.0g	1.81
Povidone, USP (<u>PLASDONE® Plasidone K30</u>)	98.0g	5.38
Sodium lauryl sulfate, NF/USP	6.0g	0.33
Microcrystalline cellulose (<u>Avicel AVICEL® PH102</u>)	1439.0g	79.07
Glipizide	244.0g	13.41
Purified water, USP	1600.0g	

Please replace the paragraph beginning at page 21, line 15 of the specification as filed with the following:

--The granulation is formed into tablets containing 10mg of glipizide by first mixing the glipizide granules with crospovidone and microcrystalline cellulose (Avicel AVICEL® PH101), then with glyceryl monostearate, as follows:--

Please replace the paragraph located at page 22, line 1 of the specification as filed with the following:

--Avicel AVICEL® PH101 16.2g—

Please replace the paragraph beginning on page 22, line 9 of the specification as filed with the following:

--A granulation comprising an antilipemic active ingredient is formed in fluid bed coater using a top spray granulation-forming suspension containing micronized active ingredient, e.g., lovastatin; 5%w/w of the total amount of L-arginine; polyvinyl pyrrolidone; sodium lauryl sulfate; a polymethacrylic acid copolymer, e.g., Eudragit EUDRAGIT® NE30D; and purified water. This suspension is sprayed onto a mixture of microcrystalline cellulose, 95%w/w of the

total amount of L-arginine and sodium starch glycolate. The formulation for making the granulation has the following composition:--

Please replace the table located on page 22 of the specification as filed with the following:

	Wt.	%
Eudragit <u>EUDRAGIT</u> [®] NE30D	33.0g	1.81
Povidone, USP (<u>PLASDONE</u> [®] <u>Plasdone</u> K30)	98.0g	5.38
Sodium lauryl sulfate, NF/USP	6.0g	0.33
Microcrystalline cellulose (<u>Avicel</u> <u>AVICEL</u> [®] PH102)	1257.0g	69.07
L-arginine, USP/FCC	182.0g	10.00
Lovastatin	244.0g	13.41
Purified water, USP	1600.0g	

Please replace the paragraph beginning at page 23, line 1 of the specification as filed with the following:

--The granulation is formed into tablets containing 10mg of lovastatin by first mixing the lovastatin granules with crospovidone and microcrystalline cellulose (Alvicel AVICEL® PH101), then with glyceryl monostearate, as follows:--

Please replace the paragraph located at page 23, line 7 of the specification as filed with the following:

--Avicel AVICEL® PH101

Please replace the paragraph beginning at page 23, line 14 of the specification as filed with the following:

--A granulation comprising an antihypertensive is formed in fluid bed coater using a top spray granulation-forming suspension containing active ingredient, e.g., felodipine; 5%w/w of the total amount of polyvinyl pyrrolidone; sodium lauryl sulfate; a polymethacrylic acid copolymer, e.g., Eudragit EUDRAGIT[®] NE30D; and purified water. This suspension is sprayed

onto a mixture of microcrystalline cellulose, 95%w/w of the total amount of sodium starch glycolate. The formulation for making the granulation has the following composition:--

Please replace the table located at page 23-24 of the specification as filed with the following:

	Wt.	%
Eudragit <u>EUDRAGIT® NE30D</u>	33.0g	1.81
Povidone, USP (<u>PLASDONE® Plasidone K30</u>)	98.0g	5.38
Sodium lauryl sulfate, NF/USP	6.0g	0.33
Microcrystalline cellulose (<u>Avicel AVICEL® PH102</u>)	1439.0g	79.07
Felodipine	244.0g	13.41
Purified water, USP	1600.0g	

Please replace the paragraph beginning at page 24, line 3 of the specification as filed with the following:

--The granulation is formed into tablets containing 10mg of felodipine by first mixing the felodipine granules with crospovidone and microcrystalline cellulose (Avicel AVICEL® PH101), then with glyceryl monostearate, as follows:--

Please replace the paragraph located at page 24, line 9 of the specification as filed with the following:

--Avicel AVICEL® PH101 16.2g--